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Substitute for form 1449B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: August 22, 2002

(use as many sheets as necessary)

Sheet	1	of	1

Complete if Known	
Application Number	09/825,989
Filing Date	04/05/2001
First Named Inventor	Jed W. Fahey
Group Art Unit	1614
Examiner Name	Cybille Delacroix-Muirheid
Attorney Docket Number	046585-0138

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	U.S. Patent Document Kind Code[2] (*if known*)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	4,191,752		Kada et al.	03-04-1980	
	A2	3,108,040		Folkers, Karl	10-22-1963	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office[3]	Number[4]	Kind Code[5] (*if known*)	Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	A3	WO	94/19948	A1	Cho et al.	09-15-1994		

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[6]
	A4	McDanell et al., "The Effect of Feeding Brassica Vegetables and Intact Glucosinolates on Mixed-Function-Oxidase Activity in the Livers and Intestines of Rats," *Fed. Chem. Toxic.*, Vol. 27, No. 5, pp. 289-293 (1989) ©Maxwell Pergamon Macmillan plc	
	A5	Graham et al., "Diet in the Epidemiology of Cancer of the Colon and Rectum," J. Natl. Cancer Inst., Vol. 61, No. 3, September 1978.	

Examiner Signature		Date Considered	1-9-03

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2]See attached Kinds of U.S. Patent Documents. [3]Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6]Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, W

Exhibit 5-G

Notice of References Cited	Application/Control No. 09/825,989	Applicant(s)/Patent Under Reexamination FAHEY ET AL.	
	Examiner Cybille Delacroix-Muirheid	Art Unit 1614	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-5,882,646	03-1999	PUSATERI et al.	424/195.1
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	1/9/03

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,989	04/05/2001	Jed W. Fahey	046585/0138	4463

22428 7590 01/16/2003

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER
DELACROIX MUIRHEI, CYBILLE

ART UNIT	PAPER NUMBER
1614	9

DATE MAILED: 01/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 09/825,989	Applicant(s) FAHEY ET AL.	
	Examiner Cybille Delacroix-Muirheid	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48-52 and 54-57* is/are allowed.

6)☒ Claim(s) *58-60,62, 63, 68-70* is/are rejected.

7)☒ Claim(s) *53,61,64-67 and 71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The following is responsive to Applicant's amendment received Oct. 22, 2002.

No claims are cancelled. New claims 68-71 are added. Claims 48-71 are currently pending.

Information Disclosure Statement

Applicant's Information Disclosure Statement received Aug. 22, 2002 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

However, the IDS received Oct. 22, 2002 has not been considered because the references have not been received. The IDS has been placed in the file.

Response to Amendment

The objection of claim 53 set forth in paragraph 1 of the office action mailed May 22, 2002 is maintained because there is no amendment authorizing the replacement of "or" with --and--.

The previous claims rejection under 35 USC 112, paragraph 2 set forth in paragraphs 2-3 of the office action mailed May 22, 2002 **is withdrawn** in view of Applicant's amendment and the remarks contained therein.

The previous claims rejections under 35 USC 102(b) and 35 USC 103(a) set forth in paragraphs 4-10 of the office action mailed May 22, 2002 **are withdrawn** in view of Applicant's amendment and the remarks contained therein.

However, Applicant's amendment necessitates the following new ground(s) of rejection.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 58, 59, 62, 63, 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al., 4,158,656 (already of record) in view of Pusateri et al., 5,882,646 and Cho et al., WO 9419948.

Jones et al. disclose a method for extracting glucosinolates, the method comprising contacting seed material (rapeseed) with an aqueous-lower alkanol (water-alcohol, i.e. ethanol)solvent solution at a temperature below 60° C and under conditions so as to prevent enzymatic degradation of the glucosinolates. Jones et al. additionally disclose that the temperature is kept below 60° C in order to prevent activation of the myrosinase. Please see claim 1; col. 1, lines 3-6; col. 4, lines 44-63.

Jones et al. do not disclose that the isolated glucosinolates are added to food; however the Examiner refers to (1) Pusateri et al., which disclose that brassica vegetables contain glucosinolates which are helpful in fighting disease. Pusateri et al. additionally disclose that glucosinolates are converted to isothiocyanates which are known chemoprotective agents. Please see col. 1, lines 12-24; and (2) Cho et al., which discloses that isothiocyanates such as sulforaphane, isolated from Brassica, are known to detoxify carcinogens. Cho et al. additionally disclose a food product which contains the sulforaphane. Please see claim 25; the abstract; pages 6-7.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Jones et al. by adding the isolated glucosinolates to food products because, in view of the prior art especially Cho et al., one of ordinary skill in the art would

reasonably expect that foods supplemented with such chemoprotective agents would serve to reduce the risk of cancer in humans. Such a modification would have been motivated by the reasonable expectation of producing a food product conferred with healthy anticancer properties.

With respect to the claimed food products (claims 68-69), it would have been obvious and well within the capability of the skilled artisan to determine the desired, conventional food products within which to incorporate the glucosinolates.

Finally, homogenization is an art-recognized result-effective variable and it would have been obvious to one of ordinary skill in the art to modify it in the method of the prior art.

Claim 71 is objected to as being dependent upon a rejected claim.

4. Claims 58, 59, 60, 63, 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anjou et al., 4,083,836 in view of Pusateri et al., 5,882,646 and Cho et al., WO 9419948.

Anjou et al. teach a method for extracting or leaching glucosinolates from seed material, the method comprising obtaining a meat fraction of the seed material and subjecting the meat fraction to a wet state at 80-100^{0}C and leaching the glucosinolates by water, wherein the temperature of the leaching is 60-80^{0}C. Please see the abstract; col. 5, lines 21-57.

Anjou et al. do not disclose that the isolated glucosinolates are added to food; however the Examiner refers to (1) Pusateri et al., which disclose that brassica vegetables contain glucosinolates which are helpful in fighting disease. Pusateri et al. additionally disclose that glucosinolates are converted to isothiocyanates which are known chemoprotective agents. Please see col. 1, lines 12-24; and (2) Cho et al., which discloses that isothiocyanates such as

sulforaphane, isolated from Brassica, are known to detoxify carcinogens. Cho et al. additionally disclose a food product which contains the sulforaphane. Please see claim 25; the abstract; pages 6-7.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Anjou by adding the isolated glucosinolates to food products because, in view of the prior art especially Cho et al., one of ordinary skill in the art would reasonably expect that foods supplemented with such chemoprotective agents would serve to reduce the risk of cancer in humans. Such a modification would have been motivated by the reasonable expectation of producing a food product conferred with healthy anticancer properties.

With respect to claim 60, Anjou et al. do not disclose that the temperature of the leach water is 100^0C; however, since Anjou et al. establish that the glucosinolate leaching process is temperature dependent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the leaching method of Anjou et al. such that the temperature is effective to result in optimum extraction of glucosinolates from the seed material. Such a modification would have been motivated by the reasoned expectation of successfully extracting glucosinolates from the seed material.

With respect to the claimed food products (claims 68-69), it would have been obvious and well within the capability of the skilled artisan to determine the desired, conventional food products within which to incorporate the glucosinolates.

Finally, homogenization is an art-recognized result-effective variable and it would have been obvious to one of ordinary skill in the art to modify it in the method of the prior art.

Claim 71 is objected to as being dependent upon a rejected claim.

Conclusion

Claims 58, 59, 60, 62, 63, 68-70 are rejected.

Claims 53, 61, 64-67, 71 are objected to.

Claims 48-57 are free from the prior art.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is (703) 306-3227. The examiner can normally be reached on Tue-Fri from 8:30 to 6:00. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

CDM

Jan. 9, 2003

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
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CHANGE OF ADDRESS/POWER OF ATTORNEY

FILE LOCATION 16RC SERIAL NUMBER 09825989 PATENT NUMBER

THE CORRESPONDENCE ADDRESS HAS BEEN CHANGED TO CUSTOMER # 22428

THE PRACTITIONERS OF RECORD HAVE BEEN CHANGED TO CUSTOMER # 22428

ON 01/13/03 THE ADDRESS OF RECORD FOR CUSTOMER NUMBER 22428 IS:

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON DC 20007

AND THE PRACTITIONERS OF RECORD FOR CUSTOMER NUMBER 22428 ARE:

25258	25479	25735	26001	26257	26874	27590	28163	28665	28822
29768	32789	32792	32904	34079	34371	34485	34702	34717	35087
35217	35264	35792	38072	38104	38819	39221	39790	40153	40413
40888	41398	41514	42322	43250	43344	43438	43445	43656	45056
45943	47131	48574							

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THIS FILE IS ASSIGNED TO GAU 1614.

Atty. Dkt. No. 046585/0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Jed FAHEY, *et al.***

Title: ***Cancer Chemoprotective Food Products***

Appl. No.: **09/825,989**

Filing Date: **April 5, 2001**

Examiner: **Cybille Delacroix-Muirhei**

Art Unit: **1614**

AMENDMENT TRANSMITTAL

MAIL STOP AF
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Transmitted herewith is an amendment in the above-identified application and:

[**X**] Small Entity status under 37 C.F.R. § 1.9 and § 1.27 has been established by a Small Entity statement previously submitted.

[**X**] Notice of Appeal.

[**X**] Copies of references as cited in PTO 1449 dated October 22, 2003 to be hand carried tomorrow.

[**X**] The fee required for additional claims is calculated below:

	Claims as Amended	Previously Paid For		Extra Claims Present		Rate		Additional Claims Fee
Total Claims:	24	24	=	0	x	$18.00	=	$0.00
Independents:	2	3	=	0	x	$84.00	=	$0.00
First presentation of any Multiple Dependent Claims:					+	$280.00	=	$0.00
						CLAIMS FEE TOTAL:	=	$0.00

[**X**] Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

Atty. Dkt. No. 046585/0138

[ ]	Extension for response filed within the first month:	$110.00	$0.00
[ ]	Extension for response filed within the second month:	$410.00	$0.00
[X]	Extension for response filed within the third month:	$930.00	$930.00
[ ]	Extension for response filed within the fourth month:	$1,450.00	$0.00
[ ]	Extension for response filed within the fifth month:	$1,970.00	$0.00
		EXTENSION FEE TOTAL:	$930.00
[X]	Notice of Appeal:	$320.00	$320.00
		CLAIMS, EXTENSION AND DISCLAIMER FEE TOTAL:	$1250.00
[X]		Small Entity Fees Apply (subtract ½ of above):	$625.00
		TOTAL FEE:	$625.00

[ ] Please charge Deposit Account No. 19-0741 in the amount of $.00. A duplicate copy of this transmittal is enclosed.

[X] A check in the amount of $625.00 is enclosed.

[X] The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date July 16, 2003

By Richard Peet

FOLEY & LARDNER
Customer Number: 22428
22428
PATENT TRADEMARK OFFICE
Telephone: (202) 672-5483
Facsimile: (202) 672-5399

Richard C. Peet
Attorney for Applicant
Registration No. 35,792

Atty. Dkt. No. 046585/0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Jed FAHEY, et al.**

Title: ***Cancer Chemoprotective Food Products***

Appl. No.: **09/825,989**

Filing Date: **April 5, 2001**

Examiner: **C. Delacroix Muirhei**

Art Unit: **1614**

AMENDMENT AND REPLY UNDER 37 C.F.R. §1.116

Commissioner for Patents
BOX AF
Washington, D.C. 20231

Sir:

In reply to the *Final* Office Action mailed January 16, 2003, the due date for response having been extended three month(s) to July 16, 2003, Applicants submit the following Amendment and Reply under 37 C.F.R. § 1.116.

Applicants concurrently file herewith a Petition for Extension of Time under 37 C.F.R. § 1.136(a), with provision for the required fee, to extend the period for response for three month(s), up to and including July 16, 2003. If additional fees are necessary to prevent abandonment of this application, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741.

IN THE CLAIMS:

In accordance with 37 C.F.R. § 1.121, please substitute for claim 53 the following rewritten version of the same claim, as amended. The changes are shown explicitly in the attached "Version with Markings to Show Changes Made".

53. (Amended) The method of claim 52, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants and plant parts.

REMARKS

Status of the Claims

By this amendment, claim 53 is amended. Upon entry of this Amendment, claims 48-71 will remain pending in the application.

Information Disclosures Statement

The Examiner asserts that the IDS received August 22, 2002 has been considered. However, the Examiner assets that the IDS received October 22, 2002 has not been considered because the references have not been received. Applicants submitted copies of these references on October 22, 2003. However, for the convenience of the Examiner, provided herewith are additional copies of the references cited in the IDS received on October 22, 2002. A copy of A47 will be provided in the near future.

Claim Objections

Claim 53 is objected to by the Examiner because the claim contains an improper Markush group. Applicants have amended claim 53 by replacing "or" with --and--. Applicants respectfully request withdrawal of the rejection.

Claim Rejections - 35 U.S.C. § 103

A. Claims 58, 59, 62, 63 and 68-70 are rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Jones et al. (U.S. Patent No. 4,158,656) in view of Pusateri et al. (U.S. Patent No. 5,882,646) and Cho et al. (WO 94/19948). The Examiner asserts that Jones et al. disclose a method for extracting glucosinolates; however, Jones et al. does not disclose that the isolated glucosinolates are added to food. The Examiner asserts that since Pusateri et al. discloses that brassica vegetables contain glucosinolates which are helpful in fighting disease and Cho et al. discloses that isothiocyanates isolated from Brassica are known to detoxify cracinogens, it would have been obvious for a person of ordinary skill in the art to modify the method of Jones et al. by adding the isolated glucosinolates to food products. Applicants respectfully disagree with the Examiner and request reconsideration and withdrawal of the rejection.

A proper rejection for obviousness under §103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, or device, or carry out the claimed process and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. [emphasis added] *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991).

In the pending case, the Examiner has failed to establish a *prima facie* case of obviousness because neither of the above recited factors are met by the teachings of Jones et al. in view of Pusateri et al. and Cho et al. This is because the primary reference that the Examiner is applying, Jones et al., teaches away from the presently claimed method. The present specification teaches that most of the Phase 2 inducer potential of crucifer plants is due to their content of isothiocyanates and their biogenic precursors, glucosinolates. See page 15, lines 3-6. Thus, the present method is directed to recovering glucosinolates and isothiocyanates and adding these compounds to food. In contrast, in column 1, lines 7-13 of Jones et al., it

states that "certain oilseeds...contain thioglucosides (glucosinolates) which, by means of endogenic enzymes, e.g. myrosinases, are split into the deleterious substances isothiocyanates and/or oxazolidinethiones, and glucose and bisulphate." In column 3, lines 40-44, Jones et al. states "[t]he glucosinolates contained in rapeseed are, as is well known, hydrolyzed by myrosinase under the appropriate conditions to isothiocyanates, nitriles and oxazolidinethiones some of which are known to cause goiter." Jones et al. also states at column 3, lines 48-53 that "it is essential for food use, to remove the glucosinolates and those other factors that can cause unattractive flavor and coloration and decreased nutritive value of foods." As such, Jones et al. explicitly teaches away from adding glucosinolates to food products. Therefore, Jones et al. teaches away from the present invention.

Applicants remind the Examiner that is it improper to take individual teachings from one reference out of context (Jones et al.) and to combine those individual teachings with teachings from other references (Pusateri et al. and Cho et al.) to make an obviousness rejection. Instead, the Examiner must consider Jones et al. in its entirety. As discussed above, Jones et al. explicitly teaches removing glucosinolates from food because of their deleterious properties, such as decreased nutritive value and unattractive flavor. Because Jones et al. teaches away from adding glucosinolates to food, the prior art would not have suggested to those of ordinary skill in the art that they should modify the Jones et al. method by adding the isolated glucosinolates to food products, as the Examiner alleges is suggested by Pusateri et al. and Cho et al. Additionally, because Jones et al. teaches away from adding glucosinolates to food, those of ordinary skill would not have a reasonable expectation of success in combining the teachings of Jones et al. with the teachings of Pusateri et al. and Cho et al.

B. Claims 58, 59, 60, 63, and 68-70 re rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Anjou et al. (U.S. Patent No. 4,083,836) in view of Pusateri et al. (U.S. Patent No. 5,882,646) and Cho et al. (WO 94/19948). The Examiner asserts that Anjou et al. teach a method for extracting or leaching glucosinolates from seed material; however, Anjou et al. does not disclose that the isolated glucosinolates are added to food. The Examiner asserts that since Pusateri et al. discloses that brassica vegetables contain glucosinolates which are helpful in fighting disease and Cho et al. discloses that

isothiocyanates isolated from Brassica are known to detoxify cracinogens, it would have been obvious for a person of ordinary skill in the art to modify the method of Anjou et al. by adding the isolated glucosinolates to food products. Applicants respectfully disagree with the Examiner and request reconsideration and withdrawal of the rejection.

A proper rejection for obviousness under §103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, or device, or carry out the claimed process and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. [emphasis added] *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991).

In the pending case, the Examiner has failed to establish a *prima facie* case of obviousness because neither of the above recited factors are met by the teachings of Anjou et al. in view of Pusateri et al. and Cho et al. This is because, as discussed above with respect to Jones et al., the primary reference that the Examiner is applying, Anjou et al., teaches away from the presently claimed method. Anjou et al. emphasizes the necessity of removing glucosinolates from seeds of Brassica species in order to produce a protein concentrate "which is non-toxic, has an acceptable light color, a neutral and mild flavor and a high nutritional value and which thus is well suited for human consumption." See column 1, lines 8-11. In column 1, lines 21-28, Anjou et al. discusses the drawbacks of prior art oil extractions which contained "glucosinolates, which could be split into deleterious compounds with pungent flavor." Anjou et al. therefore teaches away from the present method by emphasizing the necessity of removing glucosinolates from Brassica seeds in order to produce a non-toxic protein concentrate that is suited for human consumption.

Applicants remind the Examiner that is it improper to take individual teachings from one reference out of context (Anjou et al.) and to combine those individual teachings with teachings from other references (Pusateri et al. and Cho et al.) to make an obviousness rejection.

Instead, the Examiner must consider Anjou et al. in its entirety. As discussed above, Anjou et al. explicitly teaches removing glucosinolates from food because of their deleterious properties, such as being unsuitable for human consumption and having an unattractive flavor. Because Anjou et al. teaches away from adding glucosinolates to food, the prior art would not have suggested to those of ordinary skill in the art that they should modify the Anjou et al. method by adding the isolated glucosinolates to food products, as the Examiner alleges is suggested by Pusateri et al. and Cho et al. Additionally, because Anjou et al. teaches away from adding glucosinolates to food, those of ordinary skill would not have a reasonable expectation of success in combining the teachings of Anjou et al. with the teachings of Pusateri et al. and Cho et al.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

Applicants believe the application is in condition for allowance. However, in order to maintain pendency of the application, Applicants are filing a Notice of Appeal.

If the Examiner has any questions concerning this application, he or she is requested to contact the undersigned.

Respectfully submitted,

Date July 16, 2003

By Richard C. Peet

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5483
Facsimile: (202) 672-5399

Richard C. Peet
Attorney for Applicants
Registration No. 35,792

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

53. (Amended) The method of claim 52, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants [or] and plant parts.

AF/1614

#11 JRP 7/22/03

Atty. Dkt. No 046225/0128

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Jed FAHEY, *et al.***

Title: ***Cancer Chemoprotective Food Products***

Appl. No.: **09/825,989**

Filing Date: **April 5, 2001**

Examiner: **Cybille Delacroix-Muirhei**

Art Unit: **1614**

PETITION FOR EXTENSION OF TIME

MAIL STOP AF
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicant hereby petitions the Commissioner under 37 C.F.R. 1.136(a) for a three-month extension of time for response in the above-identified application for the period required to make the attached response timely.

The extension fee for response within the third month is $465.00. A check for this amount is enclosed herewith.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 16, 2003

By Richard C. Peet

FOLEY & LARDNER
Customer Number: 22428

22428
PATENT TRADEMARK OFFICE

Telephone: (202) 672-5483
Facsimile: (202) 672-5399

Richard C. Peet
Attorney for Applicant
Registration No. 35,792

07/17/2003 HDEMESS1 00000041 09825989
02 FC:2253 465.00 OP

002.1035448.1

#12 JRR 7/22/03

Atty. Dkt. No. 046585/0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Jed FAHEY, *et al.***

Title: ***Cancer Chemoprotective Food Products***

Appl. No.: **09/825,989**

Filing Date: **April 5, 2001**

Examiner: **Cybille Delacroix-Muirhei**

Art Unit: **1614**

NOTICE OF APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

MAIL STOP AF
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicant hereby appeals to the Board of Patent Appeals from the decision of the final rejection dated January 16, 2003, of the Examiner finally rejecting Claims 58-60, 62, 63, and 68-70.

[X] Applicant claims small entity status.

[X] Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

[X] Notice of Appeal Fee

[X]To be paid as detailed below

[ ]Not required (Fee paid in prior appeal)

07/17/2003 HDEMESS1 00000041 09825989
01 FC:2401 160.00 OP

The required fees are calculated below:

[X]	Notice of Appeal Fee	$320.00
[X]	Extension for response filed within the third month:	$930.00
[ ]	Extension:	$0.00
	FEE TOTAL:	$1250.00
[X]	Small Entity Fees Apply (subtract ½ of above):	$625.00
	TOTAL FEE:	$625.00

[ ] Please charge Deposit Account No. 19-0741 in the amount of $.00 . A duplicate copy of this transmittal is enclosed.

[X] A check in the amount of $625.00 is enclosed.

[X] The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date July 16, 2003

By Richard C Peet

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Richard C. Peet
Attorney for Applicant
Registration No. 35,792

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,989	04/05/2001	Jed W. Fahey	046585/0138	4463

22428 7590 11/19/2003

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,989	FAHEY ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☒ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *48-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48-57 and 59-71* is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The following is responsive to the amendment received July 16, 2003.

No claims are cancelled. No new claims are added. Claims 48-71 are currently pending.

The previous claim rejections set forth in paragraphs 1-4 of the office action mailed Jan. 16, 2003 is withdrawn in view of Applicant's amendment and the remarks contained therein.

This application is in condition for allowance except for the following formal matters:

Claim 58 is objected to because at line 3, after "glucosinolates" and before "recovering", the term –isothiocyanates—should be added.

Prosecution on the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

A shortened statutory period for reply to this action is set to expire **TWO MONTHS** from the mailing date of this letter.

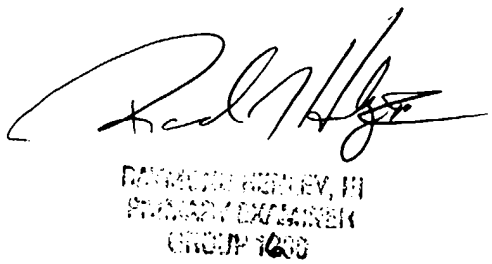
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Mon-Fri. from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725 The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

Nov. 17, 2003



IN THE CLAIMS:

In accordance with 37 C.F.R. § 1.121, please substitute for claim 53 the following rewritten version of the same claim, as amended. The changes are shown explicitly in the attached "Version with Markings to Show Changes Made".

53. (Amended) The method of claim 52, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants and plant parts.

REMARKS

Status of the Claims

By this amendment, claim 53 is amended. Upon entry of this Amendment, claims 48-71 will remain pending in the application.

Information Disclosures Statement

The Examiner asserts that the IDS received August 22, 2002 has been considered. However, the Examiner assets that the IDS received October 22, 2002 has not been considered because the references have not been received. Applicants submitted copies of these references on October 22, 2003. However, for the convenience of the Examiner, provided herewith are additional copies of the references cited in the IDS received on October 22, 2002. A copy of A47 will be provided in the near future.

Claim Objections

Claim 53 is objected to by the Examiner because the claim contains an improper Markush group. Applicants have amended claim 53 by replacing "or" with --and--. Applicants respectfully request withdrawal of the rejection.

[redacted]

SEARCHED

Class	Sub.	Date	Exmr.
426 ↓	425 429 431 615 ↓	5/1/02 ↓	cmm ↓
updated		1/9/03	cmm
upd called		11/16/03	cmm

INTERFERENCE SEARCHED

Class	Sub.	Date	Exmr.

SEARCH NOTES (INCLUDING SEARCH STRATEGY)

	Date	Exmr.
EAST (search history in file)	5/1/02 ↓	cmm ↓
EAST update	1/9/03	cmm
EAST update	11/16/03	cmm

ISSUE SLIP STAPLE AREA (for additional cross references)

POSITION	INITIALS	ID NO.	DATE
FEE DETERMINATION			
O.I.P.E. CLASSIFIER			
FORMALITY REVIEW	AK	931	05/30/01
RESPONSE FORMALITY REVIEW			

INDEX OF CLAIMS

✔	Rejected	N	Non-elected
=	Allowed	I	Interference
–	(Through numeral)... Canceled	A	Appeal
÷	Restricted	O	Objected

Claim		Date		
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If more than 150 claims or 10 actions staple additional sheet here

Atty. Dkt. No. 046585/0138

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jed W. FAHEY, et al.

Title: *Cancer Chemoprotective food Products*

Appl. No.: 09/825,989

Filing Date: April 5, 2001

Examiner: C. Delacroix Muirhel

Art Unit: 1614

REPLY TO *Ex Parte Quayle ACTION*

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

This communication is responsive to the *Ex Parte Quayle* Office Action dated November 19, 2003, concerning the above-referenced patent application.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this document.

Remarks/Arguments begin on page 5 of this document.

Please amend the application as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-47. (Canceled)

48. (Previously Presented) A method of extracting glucosinolates and isothiocyanates from plant tissue comprising homogenizing said plant tissue in an excess of a mixture of dimethyl sulfoxide, acetonitrile and dimethylformamide at a temperature sufficient to inactivate myrosinase enzyme activity.

49. (Previously Presented) The method of claim 48, wherein the ratio of dimethyl sulfoxide:acetonitrile:dimethylformamide is 1:1:1.

50. (Previously Presented) The method of claim 48, wherein said temperature is between 0°C and the freezing temperature of the extraction mixture.

51. (Previously Presented) The method of claim 48, wherein said temperature is between -50°C and the freezing temperature of the extraction mixture.

52. (Previously Presented) The method of claim 48, wherein said plant tissue is rich in glucosinolates.

53. (Previously Presented) The method of claim 52, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants or plant parts.

54. (Previously Presented) The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

55. (Previously Presented) The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 300,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

56. (Previously Presented) The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 400,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

57. (Previously Presented) The method of claim 53, wherein said sprouts, seeds, plants or plant parts have at least 500,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

58. (Currently Amended) A method of making a food product comprising extracting glucosinolates and isothiocyanates from plant tissue having a high concentration of glucosinolates and isothiocyanates, recovering said glucosinolates and isothiocyanates and adding said glucosinolates and isothiocyanates to food;

wherein said extracting comprises contacting said plant tissue with a non-toxic solvent at a temperature sufficient to inactivate myrosinase enzyme activity.

59. (Previously Presented) The method according to claim 58, wherein said solvent is water.

60. (Previously Presented) The method of claim 59, wherein said water is 100°C.

61. (Previously Presented) The method according to claim 58, wherein said solvent is liquid carbon dioxide.

62. (Previously Presented) The method according to claim 58, wherein said solvent is ethanol.

63. (Previously Presented) The method of claim 58, wherein said plant tissue is selected from the group consisting of cruciferous sprouts measured after 3 days of growth, cruciferous seeds, plants and plant parts.

64. (Previously Presented) The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

65. (Previously Presented) The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 300,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

66. (Previously Presented) The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 400,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

67. (Previously Presented) The method of claim 63, wherein said sprouts, seeds, plants or plant parts have at least 500,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

68. (Previously Presented) The method of claim 58 wherein said food product is selected from the group consisting of a bread, a drink, a soup, a salad, a sandwich and a cereal.

69. (Previously Presented) The method of claim 68 wherein said drink is a tea.

70. (Previously Presented) The method of claim 58 wherein said extracting further comprises homogenizing said plant tissue with said non-toxic solvent.

71. (Previously Presented) The method of claim 63 wherein said sprouts, seeds, plants or plant parts have at least 250,000 units per gram fresh weight of Phase 2 enzyme-inducing potential.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 58 is currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Upon entry of this Amendment, claims 48-71 will remain pending in the application.

The Examiner objected to claim 58 and states that at line 3, after "glucosinolates" and before "recovering," the term --isothiocyanates-- should be added. Applicants have amended the claim as suggested by the Examiner. Exemplary support for the amendment is found throughout the specification. *See, e.g.,* page 22, lines 18-28 and page 7, line 34, through page 8, line 8. Applicants respectfully request withdrawal of the objection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of

papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date January 20, 2004 (Tuesday after Holiday)

By _____ Reg. No. 34,985

for Richard C. Peet
Attorney for Applicant
Registration 35,792

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125487

Access DB# _____

Shear

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: C. Delacroix Examiner #: 71100 Date: 6-22-(

Art Unit: 1614 Phone Number 272-0572 Serial Number: 09/825,989

Mail Box and Bldg/Room Location: 4C85 (office) 4C70 (mailbox) Results Format Preferred (circle): PAPER DISK E-

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

PLEASE SEE ATTACHED

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search claims 45 + 58.

Key terms are highlighted.

Rush Search Approved

SPE, AU 1615

Thanks

CDx

Please rush - Than

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STAFF USE ONLY

Searcher _____

Type of Search 5-G39

NA Sequence (#) _____ STN _____

Vendors and cost where applicable

Delacroix
09/825989


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     FILE 'REGISTRY' ENTERED AT 12:07:49 ON 24 JUN 2004
                E ISOTHIOCYANATE/CN 5
L1            1 SEA ABB=ON  PLU=ON  ISOTHIOCYANATE/CN
                E GLUCOSINOLATE/CN 5
                E MYROSINASE/CN 5
L2            1 SEA ABB=ON  PLU=ON  MYROSINASE/CN

     FILE 'CAPLUS' ENTERED AT 12:08:58 ON 24 JUN 2004
L3        32844 SEA ABB=ON  PLU=ON  L1 OR ISOTHIOCYANATE OR ISO(W)(THIOCY
                ANATE OR THIO CYANATE) OR ISOTHIO CYANATE OR GLUCOSINOLAT
                E
L4          515 SEA ABB=ON  PLU=ON  L3 AND (L2 OR MYROSINASE)

     FILE 'REGISTRY' ENTERED AT 12:10:50 ON 24 JUN 2004
                E DIMETHYLSULFOXIDE/CN 5
                E DIMETHYL SULFOXIDE/CN 5
L5            1 SEA ABB=ON  PLU=ON  "DIMETHYL SULFOXIDE"/CN
                E ACETONITRILE/CN 5
L6            2 SEA ABB=ON  PLU=ON  (ACETONITRILE/CN OR "ACETONITRILE
                (13CH3CN)"/CN)
                E DIMETHYLFORMAMIDE/CN 5
L7            1 SEA ABB=ON  PLU=ON  DIMETHYLFORMAMIDE/CN

     FILE 'CAPLUS' ENTERED AT 12:11:31 ON 24 JUN 2004
L8            0 SEA ABB=ON  PLU=ON  L4 AND (L5 OR DIMETHYLSULFOXIDE OR
                DIMETHYLSULPHOXIDE OR DI(W)(METHYLSULFOXIDE OR METHYLSULP
                HOXIDE OR (ME OR METHYL)(W)(SULFOXIDE OR SULPHOXIDE)) OR
                DIMETHYL(W)(SULFOXIDE OR SULPHOXIDE))
L9           12 SEA ABB=ON  PLU=ON  L4 AND (L6 OR ACETONITRILE OR ACETO
                NITRILE)
L10           1 SEA ABB=ON  PLU=ON  L4 AND (L7 OR DIMETHYLFORMAMIDE OR
                DI(W)(METHYLFORMAMIDE OR (ME OR METHYL)(W)FORMAMIDE) OR
                DIMETHYL FORMAMIDE)
L11          12 SEA ABB=ON  PLU=ON  L9 OR L10

L11  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2004 ACS on STN
ED   Entered STN:  26 Oct 2001
ACCESSION NUMBER:         2001:780211  CAPLUS
DOCUMENT NUMBER:          136:262229
TITLE:                    Hydrolysis products of glucosinolates
                          from white cabbage (Brassica oleracea L. var
                          capitata) and cauliflower (Brassica oleracea L.
                          var botrytis) analyzed by HPLC and GC/MS
AUTHOR(S):                Delonga, Karmela; Smit, Zdenko; Dragovic-Uzelac,
                          Verica; Mrkic, Vlatka; Vorkapic-Furac, Jasna
CORPORATE SOURCE:         Faculty of Food Technology and Biotechnology,
                          University of Zagreb, Zagreb, HR-10000, Croatia
SOURCE:                   Special Publication - Royal Society of Chemistry
                          (2001), 269(Biologically-Active Phytochemicals
                          in Food), 213-216
                          CODEN: SROCDO; ISSN: 0260-6291
PUBLISHER:                Royal Society of Chemistry
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   In this study the determination of glucosinolates (GSL) in cabbage
     and cauliflower, as well as their autolysis and hydrolysis products
```

obtained by exogenous enzyme **myrosinase** was performed by reversed-phase high performance liquid chromatog. (RP-HPLC) followed by gas-chromatog./mass spectrometry (GS/MS). The anal. data of the autolysis and hydrolysis products (pH 7.0) obtained by HPLC (DAD and FL detection) and GC/MS confirmed that their relationship depends on GSL precursors and conditions of their enzymic degradation (autolysis and hydrolysis). An examination of the indole GSL degradation products showed the presence of four to seven different compds. Three of them were identified as indole-3-carbinol (13C), indole-3-**acetonitrile** (13CN) and 3,3'-diindolylmethane (DIM).

IT **9025-38-1, Myrosinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrolysis products of **glucosinolates** from white cabbage and cauliflower analyzed by HPLC and GC/MS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 28 Jun 2001
ACCESSION NUMBER: 2001:465523 CAPLUS
DOCUMENT NUMBER: 135:192989
TITLE: Jasmonate-dependent induction of indole **glucosinolates** in Arabidopsis by culture filtrates of the nonspecific pathogen Erwinia carotovora
AUTHOR(S): Brader, Gunter; Tas, Eva; Palva, E. Tapio
CORPORATE SOURCE: Department of Biosciences, University of Helsinki, Helsinki, FIN-00014, Finland
SOURCE: Plant Physiology (2001), 126(2), 849-860
CODEN: PLPHAY; ISSN: 0032-0889
PUBLISHER: American Society of Plant Physiologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Elicitors from the plant pathogen Erwinia carotovora trigger coordinate induction of the tryptophan (Trp) biosynthesis pathway and Trp oxidizing genes in Arabidopsis. To elucidate the biol. role of such pathogen-induced activation we characterized the production of secondary defense metabolites such as camalexin and indole **glucosinolates** derived from precursors of this pathway. Elicitor induction was followed by a specific increase in 3-indolylmethylglucosinolate (IGS) content, but only a barely detectable accumulation of the indole-derived phytoalexin camalexin. The response is mediated by jasmonic acid as shown by lack of IGS induction in the jasmonate-insensitive mutant coi1-1. In accordance with this, Me jasmonate was able to trigger IGS accumulation in Arabidopsis. In contrast, ethylene and salicylic acid seem to play a minor role in the response. They did not trigger alterations in IGS levels, and Me jasmonate- or elicitor-induced IGS accumulation in NahG and ethylene-insensitive ein2-1 mutant plants was similar as in the wild type. The breakdown products of IGS and other **glucosinolates** were able to inhibit growth of E. carotovora. The results suggest that IGS is of importance in the defense against bacterial pathogens.

IT **9025-38-1, Myrosinase**
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)
(jasmonate-dependent induction of indole **glucosinolates** in Arabidopsis by culture filtrates of the nonspecific pathogen Erwinia carotovora)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Jun 1999
ACCESSION NUMBER: 1999:350134 CAPLUS
DOCUMENT NUMBER: 131:127727
TITLE: Induction of auxin biosynthetic enzymes by jasmonic acid and in clubroot diseased Chinese cabbage plants
AUTHOR(S): Grsic, Slobodanka; Kirchheim, Brigitte; Pieper, Kerstin; Fritsch, Monika; Hilgenberg, Willy; Ludwig-Muller, Jutta
CORPORATE SOURCE: Botanisches Institut, Johann Wolfgang Goethe-Universitat, Frankfurt, D-60054, Germany
SOURCE: Physiologia Plantarum (1999), 105(3), 521-531
CODEN: PHPLAI; ISSN: 0031-9317
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nitrilase (NIT) and **myrosinase** are important enzymes for auxin biosynthesis in Brassicaceae, synthesis which is increased during clubroot disease. Therefore, NIT and **myrosinase** levels during club development and possible regulation mechanisms were investigated. In addition, the occurrence of different nitrilase isoforms in Chinese cabbage has been shown. Nitrilase activity was enhanced in infected roots during later stages of club development (35-42 days after inoculation). However, no differences in nitrilase mRNA levels between infected and healthy roots were found during symptom development. **Myrosinase** expression was increased in clubbed roots at slightly earlier time points (28 days after inoculation) and also at later time points during infection. The activities of tryptophan-oxidizing enzyme (TrpOxE), which catalyzes the first step in tryptophan-dependent auxin biosynthesis in Brassicaceae, and nitrilase were enhanced after treatment with jasmonic acid (JA) and Me jasmonate. Similarly, the amount of **myrosinase** mRNA was increased by JA. During clubroot disease the endogenous concentration of JA increased in infected roots 3-5 wk after inoculation. From these results it can be concluded that: (1) de novo indole-3-acetic acid (IAA) biosynthesis plays a role for symptom development of clubroot disease in Brassicaceae during later developmental stages; and (2) JA, which increased during club development, may be involved in the up-regulation of three enzymes important for IAA synthesis.
IT **9025-38-1, Myrosinase**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(induction of auxin-forming enzymes in Chinese cabbage plants by jasmonic acid and in clubroot disease)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L11 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 Jan 1999
ACCESSION NUMBER: 1999:61408 CAPLUS
DOCUMENT NUMBER: 130:167342
TITLE: Development of a new method for the evaluation of heavy volatile **glucosinolate** decomposition products
AUTHOR(S): Froehlich, G.; Fingerling, G.; Hanke, A.; He, H.; Schnitzler, W. H.
CORPORATE SOURCE: TU Munich, Freising-Weihenstephan, D-85350, Germany
SOURCE: Lebensmittelchemie (1999), 53(1), 5-6
CODEN: LEBEE2; ISSN: 0937-1478
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: German
AB A new method was developed for the enrichment of heavy volatile **glucosinolate** decomposition products. **Glucosinolates** were separated from (Brassica oleracea convar. acephala var. sabellica) after deactivation of the **myrosinase** and were metabolized by addition of external **myrosinase**. The identification of the **glucosinolate** decomposition products was performed by GC/MS. A great influence of the pH during incubation was noticed. The broadest spectrum of decomposition products was found when the pH was equal to the vegetable extract (pH=5.8). 2-Propenyl-ITC, 2-phenylethyl-ITC, 1-cyano-2,3-epithiopropan, and 3-indolylmethylcyanide were detected at every pH. Independent of the pH during incubation, 5-vinyloxazolidin-2-thion, 3-methylthiopropyl-ITC, and 3-indolmethylcyanide were detectable for the 1st time.
IT **9025-38-1, Myrosinase**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(determination of heavy volatile **glucosinolate** decomposition products in kale)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 31 Oct 1997
ACCESSION NUMBER: 1997:687616 CAPLUS
DOCUMENT NUMBER: 127:277421
TITLE: Enzymic, Chemical, and Thermal Breakdown of 3H-Labeled Glucobrassicin, the Parent Indole **Glucosinolate**
AUTHOR(S): Chevolleau, Sylvie; Gasc, Nicole; Rollin, Patrick; Tulliez, Jacques
CORPORATE SOURCE: Laboratoire des Xenobiotiques, INRA, Toulouse, 31931, Fr.
SOURCE: Journal of Agricultural and Food Chemistry (1997), 45(11), 4290-4296
CODEN: JAFCAU; ISSN: 0021-8561

Searcher : Shears 571-272-2528

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The enzymic, chemical, and thermal breakdown pathways of glucobrassicin, the major indolylmethyl **glucosinolate** of cruciferous vegetables, have been studied using synthetic 3H-labeled glucobrassicin (GBS). Radio-HPLC was used to analyze qual. and quant. the resulting products as well as their kinetics of formation. Enzymic breakdown of GBS under **myrosinase** action gave rise to different indole compds. [indole-3-carbinol (I3C), indole-3-**acetonitrile** (IAN), and 3,3'-diindolylmethane (DIM)]. At neutral pH, GBS degradation was almost complete after 1 h, and the major breakdown product was I3C, which could be converted to DIM. The formation of this self-condensation product was observed as photosensitive. In acidic conditions, enzymic degradation of GBS was a slower phenomenon, requiring 24 h to be nearly complete. IAN and I3C were the only 2 products occurring, and it was observed that the light had no effect either on the rate of formation or on the relative proportions of the breakdown products observed GBS appeared as a very stable compound since no chemical degradation could be observed after 2 h in different aqueous media with pH in the 2-11 range. Moreover, after exposure to heat treatment, GBS was weakly degraded (10% in 1 h), giving rise to a new minor indole condensation product corresponding to a 3-indolylmethylglucobrassicin (IM-GBS).
IT **9025-38-1, Myrosinase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(enzymic and chemical and thermal breakdown of 3H-labeled glucobrassicin, parent indole **glucosinolate**)

L11 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Oct 1997
ACCESSION NUMBER: 1997:625038 CAPLUS
DOCUMENT NUMBER: 127:292314
TITLE: Broccoli sprouts: an exceptionally rich source of inducers of enzymes that protect against chemical carcinogens
AUTHOR(S): Fahey, Jed W.; Zhang, Yuesheng; Talalay, Paul
CORPORATE SOURCE: Brassica Chemoprotection Laboratory and Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(19), 10367-10372
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction of phase 2 detoxication enzymes [e.g., glutathione transferases, epoxide hydrolase, NAD(P)H: quinone reductase, and glucuronosyltransferases] is a powerful strategy for achieving protection against carcinogenesis, mutagenesis, and other forms of toxicity of electrophiles and reactive forms of oxygen. Since

Sept. 14 not prior art

consumption of large quantities of fruit and vegetables is associated with a striking reduction in the risk of developing a variety of malignancies, it is of interest that a number of edible plants contain substantial quantities of compds. that regulate mammalian enzymes of xenobiotic metabolism Thus, edible plants belonging to the family Cruciferae and genus Brassica (e.g., broccoli and cauliflower) contain substantial quantities of **isothiocyanates** (mostly in the form of their **glucosinolate** precursors) some of which (e.g., sulforaphane or 4-methylsulfinylbutyl **isothiocyanate**) are very potent inducers of phase 2 enzymes. Unexpectedly, 3-day-old sprouts of cultivars of certain crucifers including broccoli and cauliflower contain 10-100 times higher levels of glucoraphanin (the **glucosinolate** of sulforaphane) than do the corresponding mature plants. **Glucosinolates** and **isothiocyanates** can be efficiently extracted from plants, without hydrolysis of **glucosinolates** by **myrosinase**, by homogenization in a mixture of equal vols. of DMSO, **DMF**, and **acetonitrile** at -50°C. Exts. of 3-day-old broccoli sprouts (containing either glucoraphanin or sulforaphane as the principal enzyme inducer) were highly effective in reducing the incidence, multiplicity, and rate of development of mammary tumors in dimethylbenz(a)anthracene-treated rats. Notably, sprouts of many broccoli cultivars contain negligible quantities of indole **glucosinolates**, which predominate in the mature vegetable and may give rise to degradation products (e.g., indole-3-carbinol) that can enhance tumorigenesis. Hence, small quantities of crucifer sprouts may protect against the risk of cancer as effectively as much larger quantities of mature vegetables of the same variety.

L11 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 Nov 1996
ACCESSION NUMBER: 1996:708153 CAPLUS
DOCUMENT NUMBER: 126:6663
TITLE: Simultaneous Determination of **Isothiocyanates**, Indoles, and Oxazolidinethiones in **Myrosinase** Digests of Rapeseeds and Rapeseed Meal by HPLC
AUTHOR(S): Matthaeus, B.; Fiebig, H.-J.
CORPORATE SOURCE: Institut fuer Chemie und Physik der Fette, Bundesanstalt fuer Getreide- Kartoffel- und Fettforschung, Muenster, D-48006, Germany
SOURCE: Journal of Agricultural and Food Chemistry (1996), 44(12), 3894-3899
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB HPLC was used for the anal. of **isothiocyanates**, indoles, and oxazolidinethiones in rapeseeds and rapeseed meal. The samples were treated with **myrosinase** and the released hydrolysis products extracted with dichloromethane. The separation was performed on an RP-18 column using a gradient system with **acetonitrile** and water. Use of a programable UV detector permitted the detection of the compds. at their absorption maxima of 210 and 240 nm, resp. Response factors of eight standard compds. were calculated for 240 nm. The

contents of **glucosinolates** calculated with the results of this method showed a significant linear correlation ($r = 0.9995$; $P < 0.005$) with the contents of **glucosinolates** evaluated with the results of the HPLC method of desulfoglucosinolates.

IT **9025-38-1, Myrosinase**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(HPLC of degradation products in rapeseed **myrosinase** digests)

L11 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 04 Oct 1992
ACCESSION NUMBER: 1992:530130 CAPLUS
DOCUMENT NUMBER: 117:130130
TITLE: Formation of indole **glucosinolates** breakdown products during processing treatment in Cruciferous vegetables
AUTHOR(S): Shim, Ki Hwan; Kang, Kap Suk; Sung, Nack Kie; Seo, Kwon Il; Moon, Ju Seok
CORPORATE SOURCE: Dep. Food Sci. Technol., Gyeongsang Natl. Univ., Jinju, 660-701, S. Korea
SOURCE: Han'guk Yongyang Siklyong Hakhoechi (1992), 21(1), 49-53
CODEN: HYSHDL; ISSN: 0253-3154
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB The released amount of thiocyanate ion in Cruciferous vegetables treated by wet heat, increased with reaction time and was maximum after treatment for 30 min, but it was not changed by dry heat treatment. When samples were autolyzed by **myrosinase**, the amount of thiocyanate ion increased gradually with time was maximum after 3 h and much higher than those in the wet-treated in cabbage, decreasing in Chinese cabbage, radish, kale and mustard in that order. The generated amount of indoleacetonitrile by heat treatment increased with time and the generated amount in each sample determined was high in the order of cabbage, Chinese cabbage and radish.
IT **302-04-5**, Thiocyanate, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, from **glucosinolates** in cruciferous vegetable processing)

L11 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 Jan 1991
ACCESSION NUMBER: 1991:6975 CAPLUS
DOCUMENT NUMBER: 114:6975
TITLE: Chemistry of indole **glucosinolates**: intermediacy of indol-3-ylmethyl **isothiocyanates** in the enzymic hydrolysis of indole **glucosinolates**
AUTHOR(S): Hanley, A. Bryan; Parsley, Keith R.; Lewis, Jenny A.; Fenwick, G. Roger
CORPORATE SOURCE: Inst. Food Res., AFRC, Norwich, NR4 7UA, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1990), (8), 2273-6
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal

Searcher : Shears 571-272-2528

LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:6975
AB The enzymic hydrolysis of 1-methoxyindol-3-ylmethyl **glucosinolate** proceeds via the corresponding **isothiocyanate**, thus providing evidence for a previously unsubstantiated breakdown pathway and establishing a link with 1-methoxycyclobrassinin and related indole phytoalexins.
IT **9025-38-1, Myrosinase**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of indole **glucosinolates** by)

L11 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 25 Jun 1989
ACCESSION NUMBER: 1989:230267 CAPLUS
DOCUMENT NUMBER: 110:230267
TITLE: Determination of **glucosinolates** in oilseed rape fodder by HPLC
AUTHOR(S): Demes, H.; Marquard, R.; Zobelt, U.
CORPORATE SOURCE: Inst. Pflanzenbau Pflanzenzuecht. I, Justus Liebig Univ., Giessen, D-6300, Fed. Rep. Ger.
SOURCE: VDLUFA-Schriftenreihe (1989), 28(100 Jahre Agrarforsch. VA, Teil 2), 771-8
CODEN: VDSCEE; ISSN: 0173-8712
DOCUMENT TYPE: Journal
LANGUAGE: German
AB **Glucosinolates** of rape forage were determined by drying (60°), grinding, extraction with hot MeOH, placing the sample on a Sephadex DEAE-25 column with an internal standard (sinigrin), washing with 0.2 M NaOAc buffer, desulfatation with sulfatase, elution with H2O, injection into a HPLC column (RP 18 ODS, 200 mm), elution with H2O-**acetonitrile** (80:20), and UV detection (229 nm). The drying of samples before grinding is emphasized, to eliminate **glucosinolate** degradation Sampling methods are also discussed. Only small samples are necessary with this method, and **myrosinase** degradation is not needed. The **glucosinolate** contents of the rape green matter were not necessarily related to **glucosinolates** in the seeds.

L11 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 05 Apr 1987
ACCESSION NUMBER: 1987:99205 CAPLUS
DOCUMENT NUMBER: 106:99205
TITLE: In vitro activity of **glucosinolates** and their products against Leptosphaeria maculans
AUTHOR(S): Mithen, R. F.; Lewis, B. G.; Fenwick, G. R.
CORPORATE SOURCE: Sch. Biol. Sci., Univ. East Anglia, Norwich, NR4 7TF, UK
SOURCE: Transactions of the British Mycological Society (1986), 87(3), 433-40
CODEN: BMSTA6; ISSN: 0007-1536
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of a variety of **glucosinolates** and their hydrolysis products on the growth of L. maculans in culture were examined When hydrolyzed with **myrosinase**, reaction products

of all the **glucosinolates** tested, except progoitrin (2-hydroxy-3-butenyl **glucosinolate**), were inhibitory; 2-propenyl **isothiocyanate**, derived from sinigrin, was the most toxic. Antifungal activity of indole hydrolysis products of glucobrassicin (3-indolylmethyl **glucosinolate**) and 1-methoxy glucobrassicin are described for the first time. Levels of **glucosinolates** reported to occur in leaves of oilseed rape correspond with levels shown here to be sufficient to generate strongly antifungal hydrolysis products. The significance of these compds. in resistance to L. maculans is discussed. In this context, the presence of indole **glucosinolate** in disproportionately high levels in low-**glucosinolate** cultivars of oilseed rape is of considerable interest.

L11 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1975:472939 CAPLUS
DOCUMENT NUMBER: 83:72939
TITLE: Aryl hydrocarbon hydroxylase induction in rat tissues by naturally occurring indoles of cruciferous plants
AUTHOR(S): Loub, William D.; Wattenberg, Lee W.; Davis, David W.
CORPORATE SOURCE: Dep. Lab. Med. Pathol., Univ. Minnesota, Minneapolis, MN, USA
SOURCE: Journal of the National Cancer Institute (1940-1978) (1975), 54(4), 985-8
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The aryl hydrocarbon hydroxylase [9037-52-9] inducers indole-3-**acetonitrile** (I) [771-51-7], indole-3-carbinol [700-06-1], and 3,3'-diindolylmethane [1968-05-4] were identified as naturally occurring in three cruciferous vegetables, Brussels sprouts, cabbage, and cauliflower. These compds. were produced during the hydrolysis of indolylmethyl **glucosinolate** [4356-52-9] by the plant enzyme **myrosinase** [**9025-38-1**].
IT **9025-38-1**
RL: BIOL (Biological study)
(of crucifer, indolylmethyl **glucosinolate** hydrolysis by, aryl hydrocarbon hydroxylase inducer formation by)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CABA, AGRICOLA, FSTA, LIFESCI, CANCERLIT' ENTERED AT 12:14:49 ON 24 JUN 2004)
L12 7 S L8
L13 32 S L9
L14 7 S L10
L15 32 S L12 OR L13 OR L14
L16 16 DUP REM L15 (16 DUPLICATES REMOVED)

L16 ANSWER 1 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2004070091 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14871576
TITLE: In vitro digestion of sinigrin and glucotropaeolin by

single strains of Bifidobacterium and identification of the digestive products.
AUTHOR: Cheng D-L; Hashimoto K; Uda Y
CORPORATE SOURCE: Department of Bioproductive Sciences, Utsunomiya University, 350 Minemachi, Utsunomiya, 321-8505 Japan.
SOURCE: Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2004 Mar) 42 (3) 351-7.
Journal code: 8207483. ISSN: 0278-6915.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040212
Last Updated on STN: 20040407
Entered Medline: 20040406

AB Three strains of Bifidobacterium sp., B. pseudocatenulatum, B. adolescentis, and B. longum were studied for their ability to digest **glucosinolates**, sinigrin (SNG) and glucotropaeolin (GTL), in vitro. All strains digested both **glucosinolates** during 24-48 h cultivation, accompanied by a decline in the medium pH from 7.1 to 5.2. The digestion of **glucosinolates** by a cell-free extract prepared from sonicated cells of B. adolescentis, but not cultivated broth, increased in the presence of 0.5 mM l-ascorbic acid. Also, a time-dependent formation of allyl **isothiocyanate** (AITC) was observed when the cell-free extract was incubated with 0.25 mM SNG for 120 min at pH 7.0. These reaction features suggest that the digestive activity may have been due to an enzyme similar to **myrosinase**, an enzyme of plant origin. GC-MS analysis of the Bifidobacterial cultured broth showed that the major products were 3-butenenitrile (BCN) and phenylacetonitrile (PhACN), from SNG and GTL, respectively and nitriles, probably due to a decrease in the pH of the media. AITC and benzyl **isothiocyanate** (BzITC) were barely detectable in the broth. It was concluded that the three species of Bifidobacteria could be involved in digestive degradation of **glucosinolates** in the human intestinal tract.

L16 ANSWER 2 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:509245 SCISEARCH
THE GENUINE ARTICLE: 687HU
TITLE: Separation and purification of **glucosinolates** from crude plant homogenates by high-speed counter-current chromatography
AUTHOR: Fahey J W (Reprint); Wade K L; Stephenson K K; Chou F E
CORPORATE SOURCE: Johns Hopkins Univ, Sch Med, Dept Pharmacol & Mol Sci, Lewis B & Dorothy Cullman Canc Chemoprotect Ctr, 406 WBSB, 725 N Wolfe St, Baltimore, MD 21205 USA (Reprint); Johns Hopkins Univ, Sch Med, Dept Pharmacol & Mol Sci, Lewis B & Dorothy Cullman Canc Chemoprotect Ctr, Baltimore, MD 21205 USA; Johns Hopkins Univ, Bloomberg Sch Publ Hlth, Ctr Human

Searcher : Shears 571-272-2528

Nutr, Baltimore, MD USA; Pharma Tech Res Corp, Baltimore, MD 21212 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CHROMATOGRAPHY A, (9 MAY 2003) Vol. 996, No. 1-2, pp. 85-93.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0021-9673.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Glucosinolates** are anionic, hydrophilic plant secondary metabolites which are of particular interest due to their role in the prevention of cancer and other chronic and degenerative diseases. The separation and purification of **glucosinolates** from a variety of plant sources (e.g. seeds of broccoli, arugula and the horseradish tree), was achieved using high-speed counter-current chromatography (HSCCC). A high-salt, highly polar system containing 1-propanol-**acetonitrile**-saturated aqueous ammonium sulfate-water (1:0.5:1.2:1), was run on a semi-preparative scale and then transferred directly to preparative scale. Up to 7 g of a concentrated methanolic syrup containing about 10% **glucosinolates** was loaded on an 850-ml HSCCC column, and good separation and recovery were demonstrated for 4-methylsulfinylbutyl, 3-methyl-sulfinylpropyl, 4-methylthiobutyl, 2-propenyl and 4-(rhamnopyranosyloxy)benzyl **glucosinolates** . Multiple injections (5 to 6 times) were performed with well-preserved liquid stationary phase under centrifugal force. Pooled sequential runs with broccoli seed extract yielded about 20 g of its predominant **glucosinolate**, glucoraphanin, which was produced at >95% purity and reduced to powdered form.

L16 ANSWER 3 OF 16 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001504897 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11330806
TITLE: Direct determination of sinigrin in mustard seed without desulfatation by reversed-phase ion-pair liquid chromatography.
AUTHOR: Jen J F; Lin T H; Huang J W; Chung W C
CORPORATE SOURCE: Department of Chemistry, National Chung-Hsing University, Taichung, Taiwan.. jfjen@mail.nchu.edu.tw
SOURCE: Journal of chromatography. A, (2001 Apr 6) 912 (2) 363-8.
Journal code: 9318488.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913

AB Reversed-phase ion-pair liquid chromatography has been investigated for directly analyzing sinigrin in mustard seed without

desulfatation. After extraction by phosphate buffer (pH 7.0) from the grind-pastes of inactivated-**myrosinase** mustard seeds, sinigrin was first isolated through deproteinization and centrifugation, followed by filtration and injection into the chromatographic system. A reversed-phase C18 column was used to separate the sinigrin with an eluent of **acetonitrile** (ACN)-water (20:80) containing 0.02 M tetrabutylammonium (TBA) as the counter ion at pH 7.0. Detection was carried out with an UV detector operated at 227 nm. Factors affecting the chromatographic separation and quantitative determination, such as concentrations of TBA and ACN, and pH, were studied. The linear dynamic range is larger than three orders of magnitude and the detection limit is 0.045 mg/L. The RSD is around 3% and the recovery is 85% (3% RSD, n = 3).

L16 ANSWER 4 OF 16 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 2002:9226 CABA
DOCUMENT NUMBER: 20013149702
TITLE: Hydrolysis products of **glucosinolates** from white cabbage (Brassica oleracea L.var Capitata) and cauliflower (Brassica oleracea L.var Botrytis) analyzed by HPLC and GC/MS
AUTHOR: Delonga, K.; Smit, Z.; Dragovic[acute]-Uzelac, V.; Mrkic[acute], V.; Vorkapic[acute]-Furac, J.; Pfannhauser, W. [EDITOR]; Fenwick, G. R. [EDITOR]; Khokhar, S. [EDITOR]
CORPORATE SOURCE: Faculty of Food Technology and Biotechnology, University of Zagreb, Pierottijeva 6, HR-10000 Zagreb, Croatia.
SOURCE: Biologically-active phytochemicals in food: analysis, metabolism, bioavailability and function. Proceedings of the EUROFOODCHEM XI Meeting, Norwich, UK, 26-28 September 2001, (2001) pp. 213-216. 5 ref.
Publisher: Royal Society of Chemistry. Cambridge
Price: Book chapter; Conference paper ; <pounds>69.50
Meeting Info.: Biologically-active phytochemicals in food: analysis, metabolism, bioavailability and function. Proceedings of the EUROFOODCHEM XI Meeting, Norwich, UK, 26-28 September 2001.
ISBN: 0-85404-806-5
PUB. COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 20020111
Last Updated on STN: 20020111

AB In this study, the determination of **glucosinolates** (GSL) in cabbage and cauliflower, as well as their autolysis and hydrolysis products obtained by exogenous enzyme **myrosinase** was performed by reversed-phase high performance liquid chromatography (RP-LC) followed by gas-chromatography/mass spectrometry (GS/MS). The analysis data of the autolysis and hydrolysis products (pH 7.0) obtained by HPLC (DAD and FL detection)

and GC/MS confirmed that their relationship depends on GSL precursors and conditions of their enzymatic degradation (autolysis and hydrolysis). An examination of the indole GSL degradation products showed the presence of 4 to 7 different compounds. Three of them were identified as indole-3-carbinol (I3C), indole-3-**acetonitrile** (I3CN) and 3,3[prime]-diindolylmethane (DIM).

L16 ANSWER 5 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2000437676 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10869674
TITLE: Supercritical fluid chromatography as a method of analysis for the determination of 4-hydroxybenzylglucosinolate degradation products.
AUTHOR: Buskov S; Hasselstrom J; Olsen C E; Sorensen H; Sorensen J C; Sorensen S
CORPORATE SOURCE: Chemistry Department, Royal Veterinary and Agricultural University, Thorvaldsensvej 40, DK-1871, Frederiksberg C, Denmark.
SOURCE: Journal of biochemical and biophysical methods, (2000 Jul 5) 43 (1-3) 157-74.
Journal code: 7907378. ISSN: 0165-022X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000920

AB In the present study analytical and preparative supercritical fluid chromatography (SFC) were used for investigation of **myrosinase** catalysed degradation of 4-hydroxybenzylglucosinolate (sinalbin). Sinalbin occurs as a major **glucosinolate** in seeds of Sinapis alba L., in various mustards and other food products. The degradation products were identified and quantified by analysis based on a developed SFC method using a bare silica column. Determinations comprised transformation products of sinalbin, produced both during degradation of isolated sinalbin, and during autolysis of meal from S. alba seeds. The conditions in the developed SFC method were used as basis for the preparative SFC procedure applied for isolation of the components prior to their identification by nuclear magnetic resonance (NMR) spectroscopy. **Myrosinase** catalysed sinalbin hydrolysis resulted in the reactive 4-hydroxybenzyl **isothiocyanate** as an initial product at pH values from 3.5 to 7.5 whereas 4-hydroxybenzyl cyanide was one of the major products at low pH values. 4-Hydroxybenzyl **isothiocyanate** was found to disappear from the aqueous reaction mixtures in a few hours, as it reacted easily with available nucleophilic reagents. 4-Hydroxybenzyl alcohol was found as the product from reaction with water, and with ascorbic acid, 4-hydroxybenzylascorbigen was produced.

L16 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 97439871 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9294217

Searcher : Shears 571-272-2528

TITLE: Broccoli sprouts: an exceptionally rich source of inducers of enzymes that protect against chemical carcinogens.

AUTHOR: Fahey J W; Zhang Y; Talalay P
CORPORATE SOURCE: Brassica Chemoprotection Laboratory and Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.

CONTRACT NUMBER: P01 CA 44530 (NCI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Sep 16) 94 (19) 10367-72.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971021

AB Induction of phase 2 detoxication enzymes [e.g., glutathione transferases, epoxide hydrolase, NAD(P)H: quinone reductase, and glucuronosyltransferases] is a powerful strategy for achieving protection against carcinogenesis, mutagenesis, and other forms of toxicity of electrophiles and reactive forms of oxygen. Since consumption of large quantities of fruit and vegetables is associated with a striking reduction in the risk of developing a variety of malignancies, it is of interest that a number of edible plants contain substantial quantities of compounds that regulate mammalian enzymes of xenobiotic metabolism. Thus, edible plants belonging to the family Cruciferae and genus Brassica (e.g., broccoli and cauliflower) contain substantial quantities of **isothiocyanates** (mostly in the form of their **glucosinolate** precursors) some of which (e.g., sulforaphane or 4-methylsulfinylbutyl **isothiocyanate**) are very potent inducers of phase 2 enzymes. Unexpectedly, 3-day-old sprouts of cultivars of certain crucifers including broccoli and cauliflower contain 10-100 times higher levels of glucoraphanin (the **glucosinolate** of sulforaphane) than do the corresponding mature plants. **Glucosinolates** and **isothiocyanates** can be efficiently extracted from plants, without hydrolysis of **glucosinolates** by **myrosinase**, by homogenization in a mixture of equal volumes of **dimethyl sulfoxide**, **dimethylformamide**, and **acetonitrile** at -50 degrees C. Extracts of 3-day-old broccoli sprouts (containing either glucoraphanin or sulforaphane as the principal enzyme inducer) were highly effective in reducing the incidence, multiplicity, and rate of development of mammary tumors in dimethylbenz(a)anthracene-treated rats. Notably, sprouts of many broccoli cultivars contain negligible quantities of indole **glucosinolates**, which predominate in the mature vegetable and may give rise to degradation products (e.g., indole-3-carbinol) that can enhance tumorigenesis. Hence, small quantities of crucifer sprouts may protect against the risk of cancer as effectively as much larger quantities of mature vegetables of the same variety.

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